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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PATENT DEPARTMENT
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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/617,561	ENRIGHT ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-14,17,31-41,48,59-70,73-76,79,83,86,87,105-114,116,118,120,122-128 and 131-133* is/are pending in the application.

4a) Of the above claim(s) *31-41,48,59-70,73-76,79,83,86-87,105-114,116,118,120,122-128* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-14,17,127, and 131-133* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-8,11-14,17,31-41,48,59-70,73-76,79,83,86-87,105-114,116,118,120,122-128,131-133* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/14/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Rejections withdrawn

35 USC § 101-non-statutory subject matter

The rejection of claims 129 and 130 under 35 U.S.C. 101 has been withdrawn in view of the cancellation of these claims (see page 2 of the response filed on 02/14/2007).

Claim Rejections - 35 USC § 112 (New Matter)

Applicant's response and arguments filed on 02/14/2007 have overcome the rejection of claims 1-8, 11-14, 17, and 127 under 35 USC, 112, First paragraph (New Matter). The rejection of claims 1-8, 11-14, 17, and 127 under 35 USC, 112, First paragraph (New Matter) has been withdrawn.

Rejections Maintained

Double Patenting

Claims 1-8, 11-14, 17, and 127 are rejected under nonstatutory obviousness-type double patenting. The basis of this rejection is set forth for claims 1-8, 11-14, 17, and 127 at page 3 of the previous Office action of 18 August 2006.

The rejection of claims 1-8, 11-14, 17, and 127 is maintained. At page 3 of the response, Applicant indicates that a Terminal Disclaimer is already of record in this application having been filed on July 11, 2003. However, upon reviewing the record of the instant application, the Examiner has not been able to locate any Terminal Disclaimer or fees associated with such. Thus the rejection is maintained.

Claim Rejections - 35 USC § 112 (Written Description)

Claims 1-8, 11-14, 17, 127, 131-133 are rejected under 35 U.S.C. 112, First paragraph (Written Description) as failing to comply with the written Description requirement. The basis for this rejection is set forth for claims 1-8, 11-14, 17, 127, 131-133 of the previous Office action of 18 August 18, 2006.

The rejection of claims 1-8, 11-14, 17, 127, 131-133 is maintained. Applicant's response and arguments filed on 02/14/2007 have been fully considered but they are not persuasive.

(i) At page 4 of the response, Applicants allege that the disclosure of a patent is directed to a person of ordinary skill in the art and the things known to those of skill in the art need not be disclosed. An analog is compound with a structure that similar to that of the parent compound and that has similar or opposing metabolic effects. Hormone analogs may act either as agonists, having a similar effect, or antagonists, having a blocking effect.

Applicant's arguments have been fully considered but are not found persuasive. While Applicants have provided information regarding analogs in the specification (page 7 to 15), the specification does not disclose any information regarding the identifying characteristics for any analogues. For instance, there is no disclosure regarding the number of substitutions or deletions of nucleic acids for an analogue while still retaining its biological function. In addition, the specification and the response filed on 02/14/2007 provide numerous review articles disclosing different hormone and lytic analogues, but there are no structure/function correlations or identifying characteristics for each analogue claimed in the instant application. The reviews disclose that hormone and lytic analogues can have different functions depending on the different amino acid sequences.

For example, Raynor et al. (1993, presented at page 9 of the response) recite numerous somatostatin peptide analogues on Table 1 (page 840), and disclose different receptor affinities for each analogue. The study conducted by Raynor et al. has identified analogues of SRIF that interact selectively with each of the cloned SRIF receptors (page 843, left column, 2nd paragraph). However, Raynor has not identified the identifying characteristics correlating the structure of the somatostatin peptide analogues with their different structures. With respect to lytic peptides, changes in the helicity of lytic peptides can lead to disruption of lytic activities. For instance, Dathe et al. (1999) teach that substitutions preventing folding of melittin into a helical conformation resulted in a loss of both hemolytic and antimicrobial activity. Furthermore, incorporation of proline in the N-terminal helix of insect cerocropin A and ceropin P1 reduced activity against different bacterial strains, which correlated well with decreased helicity (page 76, left column, 1st paragraph).

Thus, Applicants have not provided the functional or structural requirements of the analogs or evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of analogs recited in the claims.

(ii) Furthermore, Applicants assert that the present specification provides ample guidance to a worker of ordinary skill in the art as to what constitutes analogs of the recited hormones:

(i) at page 6 of the response, Applicants present numerous examples of published references disclosing analogs of gonadotropin releasing hormone, also known as luteinizing hormone (LHRH).

(ii) at page 7 of the response, Applicants present numerous examples of published references disclosing analogs of Luteinizing hormone, chorionic gonadotropin and their beta subunits.

(iii) at pages 9-10 of the response, Applicants present numberous examples of published references for Follicle stimulating hormone, somatostatin, and Lamprey III luteinizing hormone releasing hormone and the sequence SEQ ID NO: 10 for the Melanocyte stimulating hormone.

(iv) at page 10 of the response, Applicants argue that the behavior of analogs of known lytic peptides is relatively predictable and that the present specification provides more than adequate disclosure to support the claim limitations directed to analogs of certain lytic peptides. In addition, Applicants allege that the specification at page 36 provides an extensive discussion of lytic peptides.

Applicant's arguments have been fully considered but are not found persuasive. Although each reference provided by applicants discloses numerous hormone analogues and lytic peptide analogues, each reference does not teach the identifying characteristics for each hormone analogue or each lytic peptide analogue. It is noted that each reference acknowledges that that changes in the structure of the hormone or the lytic peptide will lead to disruption of their biological activities. For instance, Sealfon et al. (1997, presented at page 6 of the response) teach that several thousands GnRH analogs have been synthesized to date and information on their activities for the purpose of identifying functional residues is complicated due to numerous factors, including the effects of single amino acid substitutions may be difficult to interpret. A single substitution may alter affinity and agonist activity via modification of a side chain that interacts with the binding pocket and/or by altering the conformation of the peptide and thus affecting the presentation of other peptide moieties that interact wit the receptor (page 185, left column, 2nd paragraph). In addition, Sealfon et al. conclude that although thousands of GnRH analogs have been synthesized and biologically characterized, the complexity of most analogs and the predominance of in vivo testing have complicated the task of clearly identifying

the roles of individual amino acids in ligand conformation and in receptor binding and activation (page 190, left column, left paragraph to right column, 1st paragraph). Thus the art has not been able to provide identifying structural characteristics for the amino acid sequence of GnRH to correlate with its biological function.

Moreover, Garcia-Campayo et al. (1997; presented at page 8 of the response) teach lutropin analogs are difficult to characterize because formation of the hormone-specific oligosaccharides is also dependent on the heterodimer, and only the dimmers are biologically active. Thus it is not surprising that structure function studies of these ligands are often hampered by mutagenesis-induced defects in subunit combination and secretion of the dimer (page 663, left column, end of last paragraph).

In addition, Mezo et al. (1997, presented at page 9 of the response) teach that the superior antitumor activity of GnRH-III compared with other GnRH analogs may dependent on the structural features, sequence 5-8, which are different in GnRH-III (page 3353, left column, end of last paragraph).

Furthermore, Cerpa-Poljak et al. (1993; presented at page 9 of the response) teach that FSH isoforms have different physiological functions with acidic isoforms playing an important role in grown and maintenance of ovarian follicles whereas basic isoforms appear to have an important role in dynamic events such as ovulation (page 355, right column, last paragraph).

Raynor et al. (1993, presented at page 9 of the response) recite numerous somatostatin peptide analogues on Table 1 (page 840), and disclose different receptor affinities for each analogue. The study conducted by Raynor et al. has identified analogues of SRIF that interact selectively with each of the cloned SRIF receptors (page 843, left column, 2nd paragraph). However, Raynor has not identified the identifying characteristics correlating the structure of the somatostatin peptide analogues with their different structures.

Furthermore, for lytic peptide changes in the helicity of lytic peptides can lead to disruption of lytic activities. For instance, Dathe et al. (1999) teach that substitutions preventing folding of melittin into a helical conformation resulted in a loss of both hemolytic and antimicrobial activity. Furthermore, incorporation of proline in the N-terminal helix of insect cerocropin A and ceropin P1 reduced activity against different bacterial strains, which correlated well with decreased helicity (page 76, left column, 1st paragraph).

Finally, the specification does not provide any structure/function correlations or identifying characteristics for acute phase responsive promoter, transposase, and transposon insertion sequences claimed in the instant application. In addition, Applicants have not provided the functional or structural requirements of acute phase responsive promoter, transposase, and transposon insertion sequences to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of acute phase responsive promoter, transposase, and transposon insertion sequences recited in the claims.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 1-8, 11-14, 17, 127 and 131-133 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a gene encoding a peptide comprising bLH or beta subunit of gonadotropin-releasing hormone, lamprey III luteinizing hormone releasing hormone, beta chain of luteinizing hormone, luteinizing hormone, chorionic gonadotropin, the beta subunit of chorionic gonadotropin, follicle stimulating hormone, melanocyte-stimulating hormone, or somatostatin in the first domain and a lytic peptide consisting of cecropin peptide, melittin peptide, defensin peptide, magainin peptide, or sarcotoxin peptide in the second domain, does not reasonably provide enablement for (i) analogues of these hormones in the first domain and analogues of these lytic peptides in the

second domain (ii) a gene linked to an acute-phase responsive promoter, and (iii) a vector for inserting a gene into a chromosome of a eukaryotic cell comprising (a) gene encoding a bacterial transposase, (b) two transposon insertion sequences recognized by the transposase, (c) a gene wherein the gene is between the two transposon insertion sequences; and (d) a promoter that is operably linked to said transposase gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Nature of the invention and breath of the claims

The invention is drawn to a gene encoding a peptide, wherein a hormone peptide or analogue comprises a first domain and a lytic peptide analogue comprises the second domain and a vector for inserting a gene comprising transposon insertion sequences and promotoers. The invention is broad because the recitation of claims 1 and 3 encompasses a large number of peptide analogues and claim 132 includes a large number of transposon insertion sequences and promoters.

Unpredictability and state of the art

The state of the art for the hormone peptides and lytic peptides are well established but hormone peptide analogues or lytic peptide analogues are not well characterized.

As mentioned previously in the Written Description rejection, while Applicants have provided information regarding analogs in the specification (page 7 to 15), the specification does not disclose any information regarding the identifying characteristics for any analogues. For instance, there is no disclosure regarding the number of substitutions or deletions of nucleic acids encoding an analogue while still retaining its biological function. In addition, the specification and the response filed on 02/14/2007 provide numerous review articles disclosing different hormone and lytic analogues, but there are no structure/function correlations or identifying characteristics for each analogue claimed in the instant application. Numerous references teach that changes in the structure of the hormone or the lytic peptide will lead to disruption of the hormone or lytic analogue biological activity (see for example Sealfon et al. (1997, for hormone analogues, presented at page 6 of the response, and Dathe et al., 1999, for lytic peptide analogues).

Finally, the art is silent regarding a gene encoding a peptide wherein a hormone peptide or analogue comprises a first domain and a lytic peptide analogue comprises the second domain and a gene encoding a peptide linked to an acute-phase responsive promoter, and (iii) a vector for inserting a gene into a chromosome of a eukaryotic cell comprising (a) gene encoding a bacterial transposase, (b) two transposon insertion sequences recognized by the transposase, (c) a gene wherein the gene is between the two transposon insertion sequences; and (d) a promoter that is operably linked to said transposase gene.

The amount of direction or guidance present

Applicants' disclosure is limited to the examples for administering numerous compounds wherein a hormone peptide comprises the first domain and a lytic peptide comprises the second domain (Examples 1-22, pages 9-19, and treatments 15-51, pages 19-29). However, the specification does not provide guidance or direction regarding a gene encoding a peptide wherein analogues of these hormones comprises the first domain and analogues of these lytic peptides comprises the second domain. In addition, the specification does not provide guidance regarding the identifying characteristics for any hormone peptide analogues or lytic peptide analogues.

Moreover, the specification provides little or no guidance regarding identifying characteristics for an acute-phase responsive promoter, transposon insertion sequences recognized by the transposase, and a promoter that is operably linked to said transposase gene. Finally, there is little guidance regarding a vector for inserting a gene into a chromosome of a eukaryotic cell comprising (a) gene encoding a bacterial transposase, (b) two transposon insertion sequences recognized by the transposase, (c) a gene wherein the gene is between the two transposon insertion sequences; and (d) a promoter that is operably linked to said transposase gene.

In view of these teachings in the art and the limited guidance provided in the specification, a gene encoding a peptide, wherein a hormone peptide comprises a first domain and a lytic peptide comprises the second domain is not predictable for (1) to a gene encoding a peptide, wherein a hormone peptide analogue comprises a first domain and a lytic peptide analogue comprises the second domain (2) a gene linked to an acute-phase responsive promoter, and (3) a vector for inserting a gene into a chromosome of a eukaryotic cell comprising (a) gene encoding a bacterial transposase, (b) two transposon insertion sequences

recognized by the transposase, (c) a gene wherein the gene is between the two transposon insertion sequences; and (d) a promoter that is operably linked to said transposase gene.

Working Examples

Although Applicants have provided examples for administering numerous compounds wherein a hormone peptide comprises the first domain and a lytic peptide comprises the second domain (Examples 1-22, pages 9-19, and treatments 15-51, pages 19-29), the specification does not provide any working examples for a gene encoding a peptide wherein analogues of these hormones comprise the first domain and analogues of lytic peptides comprise the second domain. In addition, there are no working examples for a gene linked to an acute-phase responsive promoter, or a vector for inserting a gene into a chromosome of a eukaryotic cell comprising (a) gene encoding a bacterial transposase, (b) two transposon insertion sequences recognized by the transposase, (c) a gene wherein the gene is between the two transposon insertion sequences; and (d) a promoter that is operably linked to said transposase gene.

The quantity of experimentation needed

Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to make/or use a gene encoding a peptide, wherein a hormone peptide analogue comprises a first domain and a lytic peptide analogue comprises the second domain. For example, a large quantity of experimentation would be required of the skilled artisan to generate the infinite number of hormone analogs and lytic peptide analogs in the claims and screen the fusion of the peptides for the desired functional activity. In addition, it would require undue experimentation to practice the invention commensurate in scope with the claims because, the claims are broadly drawn to a gene encoding a peptide, wherein a hormone

peptide or analogue comprises a first domain and a lytic peptide analogue comprises the second domain a vector for inserting a gene comprising transposon insertion sequences and promoters.

Conclusion

No claim is allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
April 24, 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER